REMARKS

Applicants have canceled claims 46-47 and have amended claims 8 and 36 to incorporate the limitations of the canceled dependent claims 46 and 47, respectively. Applicants note that the Office Action did not include an anticipation rejection of Claims 46 and 47. Applicants submit that the 35 U.S.C. § 102(b) rejection of the pending claims is rendered moot by incorporating the limitations of these claims into independent claims 8 and 36. Applicants therefore request entry of the amendments as they simplify issues for appeal by removing the 35 U.S.C. § 102(b) anticipation rejection, do not raise issues of new matter, and do not require any additional consideration or searching. Applicants note that the cancellation and amendment of these claims is done without any admission regarding patentability of the previously-claimed subject matter and reserve the right to pursue that subject matter in this or any other patent application.

Applicants thank the Examiner for his review of the pending application. Applicants acknowledge the withdrawal of the 35 U.S.C. § 102(b) rejection of the claims as anticipated by Dante. For the reasons discussed below, Applicants respectfully traverse the pending rejections.

Claim Objections

The Examiner states that newly added claims 44-45 (reciting zonisamide as a third component) are "directed to an invention that is independent or distinct from the invention originally elected invention which are drawn to a composition comprising naltrexone as 1st compound and bupropion as 2nd compound." *Office Action* at 2. The Examiner states that because Applicants have received an action on the merits for the originally selected invention, "claims 44 and 45 will be withdrawn from further consideration by the examiner as being drawn to a non-elected invention." *Id.* Applicants respectfully traverse.

As stated in 37 C.F.R. § 1.141

> Two or more independent and distinct inventions may not be claimed in one national application, except that more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form (§ 1.75) or otherwise include all the limitations of the generic claim. *37 C.F.R. § 1.141* (emphasis added).

Applicants note that claims 44 and 45 are species of the broader generic claims 8 and 36, and are written in proper dependent form from claims 8 and 36, respectively. Thus, Applicants understand that according to Rule 1.141, the Examiner should examine claims 8 and 36 and determine if Applicants are entitled to generic claims 8 and 36. If the generic claims 8 and 36 are allowed, then dependent claims 44 and 45 to species of generic claims 8 and 36 should be examined and allowed as well. If the Examiner disagrees with Applicant's understanding of the rules regarding election of species, Applicants invite the Examiner to contact the undersigned to discuss any further actions to be taken.

35 U.S.C. § 102(b) – Anticipation

The Examiner has rejected claims 8-9, 36-43 and 48-49 under 35 U.S.C. § 102(b) as being anticipated by O'Malley et al. (US Patent 6004970). Applicants respectfully traverse. Without acquiescing to the Examiner's arguments, and solely in the interest of advancing prosecution, Applicants have amended independent claims 8 and 36 to incorporate the limitations of claims 46 and 47, respectively. Applicants note that claims 46 and 47 are not rejected as anticipated by O'Malley, and therefore the inclusion of the limitations of these claims into independent claims 8 and 36 overcomes the anticipation rejection. Applicants therefore request that the Examiner withdraw the rejection of the pending claims as anticipated by O'Malley.

35 U.S.C. § 103(a) – Obviousness

Claims 8-9, 36-43 and 46-49 are rejected under 35 U.S.C. § 103(a) as being unpatentable "over Dante (USP 5817665) in view of applicant's admission of the prior art of record (para. [0100]), and further in view of Chen et al. (US6210716 B1) and Cook (US 6071918)." *Office Action* at 6. The Examiner asserts that Dante discloses a composition comprising a pharmacologically effective dose of a compound of opioid antagonists and nontricyclic antidepressants, that Applicants have admitted that various sustained-release materials have been established and are well known by those skilled in the art, and that Chen and Cook demonstrate the routine knowledge in preparing naltrexone and bupropion in controlled or sustained release formulation. *Id.* Applicants respectfully traverse. The rejection seems to simply say that out of the laundry list of materials in Dante, it would be obvious to put anything with anything, whether

sustained release or not, with no particular attention to the specific pharmacokinetics of the individual drugs. In contrast to such a scattergun approach, Applicants have determined that because the half life of bupropion is much shorter than that of naltrexone, if one desires to obtain the newly-discovered synergistic weight loss benefits of combinations of those specific drugs, the bupropion should be in sustained release form, as set forth in the present claims. No recognition of the desirability of matching the pharmacokinetics of these specific drugs is present in the cited art. Moreover, Applicants specifically disagree with the Examiner's characterization of para [0100] of the specification as an admission. For at least these reasons, no *prima facie* case of obviousness has been established. Even if it were, however, that would not be determinative here, due to unexpected synergistic results of record.

Without conceding a *prima facie* case of obviousness, Applicants direct the Examiner's attention to the previously submitted evidence that the claimed combinations of naltrexone and sustained release bupropion (buproprion SR) have unexpected properties, such that the claimed compositions are non-obvious. Applicants note that §2141 ¶ III of the M.P.E.P., titled "Objective Evidence Must Be Considered," states that: "Objective evidence or secondary considerations such as unexpected results…are relevant to the issue of obviousness and must be considered in every case in which they are present. When evidence of any of these secondary considerations is submitted, the examiner must evaluate the evidence." *M.P.E.P. §2141 ¶ III* (emphasis added). Applicants respectfully request that the Examiner evaluate the question of obviousness in light of the previously submitted evidence of record.

Pursuant to 37 C.F.R. § 1.132, Applicants previously submitted in the response filed on January 23, 2007, as Exhibit 1, a declaration of Michael A. Cowley, Ph.D., an expert in the field and co-inventor of the instant application. As Dr. Cowley's declaration states, the combination of naltrexone and bupropion SR has unexpected, non-obvious properties.

In particular, Applicants have not merely submitted anecdotal evidence of a purported benefit. Instead, Dr. Cowley reports strongly synergistic results seen in well controlled, statistically-significant human clinical trials of the combination of naltrexone and bupropion SR to treat obesity. Dr. Cowley states, in part, that for the completer population of the Phase IIb trial, between 64-70% of patients administered the combination lost at least 5% of their body weight, compared to 32% for bupropion SR alone, 15% for naltrexone alone and 20% for

placebo. *Cowley Declaration* at ¶5. Of patients receiving the combination, 24-32% of patients in the completer group lost at least 10% of their body weight, compared to 9% for bupropion SR alone, 3% for naltrexone alone and 3% for placebo. *Id.* These detailed clinical studies of record demonstrate that the combination of naltrexone and bupropion SR has synergistic effects which are unexpected in comparison to the results of the components when administered alone. Because a composition and its properties are considered together in determining obviousness (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)), and because unexpected, synergistic results are seen with the composition, any *prima facie* case of obviousness has been overcome. *See, e.g., M.P.E.P. § 2144.09* (citing *Papesch*) and *M.P.E.P. § 716.02 - § 716.02(g).*

In light of the above, Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. § 103(a) as obvious over Dante in light of Chen and Cook.

CONCLUSION

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: May 7 2007

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